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Laboratory Preparation of Alkyl Amines

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BROADLY SPEAKING, the term "alkyl amines" covers compounds containing one or more N $\left[-\overset{|}{\underset{|}{C}}-\right]_{1,\ 2,\ \text{or}\ 3}$ groups in which the carbon atom is not part of an aromatic ring system.

The successful production of alkyl amines is of primary importance because of the multiple uses which can be made of these versatile compounds. Alkyl amines are used in the laboratory and in industry as solvents, organic bases, and depilatories, and for general synthesis of drugs, dyes, plasticizers, insecticides, surface-active agents, wetting agents, dispersing agents, textile fibers (Nylon), ore flotation agents, and lubricants.

The subject of their preparation is of sufficient size and importance to fill several monographs. Because of the many synthetic methods used in the preparation of alkyl amines, the treatment given the subject in this article will, in general, be schematic.

Probably in no field of organic chemistry has the use of pressure equipment, of a catalyst, of the continuous process, or some combination of these three been more productive of satisfactory results than in the synthesis of aliphatic amines.

Contrary to views held by many, the use of a catalytic process or of pressure equipment, or of some combination of the two methods, does not lead to uncontrolled by-products when compared to such fundamental methods of synthesis as the Grignard reagent, nitration, halogenation, sulfonation, oxidation, the Friedel and Crafts reaction, and alkylation.

In general, practical synthesis of alkyl amines can be grouped under the following types of reactions, a typical example being given under each type:

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I. Group Replacement

A. (1) $RX + HN\begin{smallmatrix} R^1 \\ R^2 \end{smallmatrix} \longrightarrow R\text{-}N\begin{smallmatrix} R^1 \\ R^2 \end{smallmatrix} + HX$ (or salt thereof), wherein R is an alkyl group, R^1 and R^2 are selected from hydrogen, alkyl, aryl, or part of a hetero- or homocyclic system, and wherein X is a group selected from halogen, $-ONO_2$, phosphate, and sulfate.

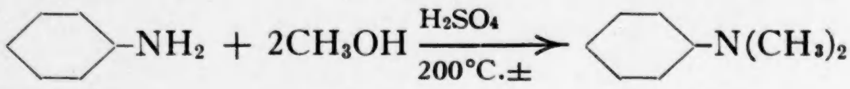
(2) Butyl chloride + Ammonia $\longrightarrow C_4H_9NH_2 + (C_4H_9)_2NH + (C_4H_9)_3N$

(3) Sodium ethyl sulfate + Ammonia $\xrightarrow[150°C.\pm]{}$ Ethylamine

B. (1) $\begin{matrix} R^1 \\ R^2 \end{matrix}\!\!>\!NH + ROH \xrightarrow{\substack{\text{Supported phosphate catalysts} \\ HF \\ HCl \\ H_2SO_4}} \begin{matrix} R^1 \\ R^2 \end{matrix}\!\!>\!N\text{–}R$

(2) Ethanol $+ \; nNH_3 \xrightarrow[300^\circ\ C.\pm]{H_3PO_4 \text{ and pressure}}$ Mono-, di-, and triethylamine

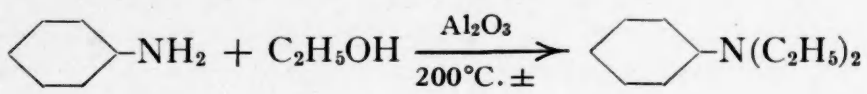
(3) Aniline + Ethanol $\xrightarrow{(BF)_3}$ Mono- and diethylaniline

(4) 

C. (1) $R\text{–}OH + H\text{–}N\begin{smallmatrix} R^1 \\ R^2 \end{smallmatrix} \xrightarrow{\text{A hydrogenation catalyst}} R\text{–}N\begin{smallmatrix} R^1 \\ R^2 \end{smallmatrix}$

(2) $C_4H_9OH + nNH_3 \xrightarrow[225^\circ C.\pm]{(Ni)}$ Butylamines

D. (1) $R\text{–}OH + H\text{–}N\begin{smallmatrix} R^1 \\ R^2 \end{smallmatrix} \xrightarrow[\text{Dehydration Catalyst } Al_2O_3\text{, etc.}]{200^\circ C +} R\text{–}N\begin{smallmatrix} R^1 \\ R^2 \end{smallmatrix}$

(2) 

(3) Methanol, dimethylether $+ \; nNH_3 \xrightarrow[300^\circ\ C.\pm]{\substack{(Al_2O_3) \\ \text{(aluminum silicate, etc.)}}}$ Mono-, di-, and trimethylamine

E. (1) Hydroxy aromatic $+ \; R\text{–}NH_2 \xrightarrow{200^\circ C\pm} \text{Aryl–}\overset{H}{\underset{|}{N}}\text{–R}$

Hydroquinone + Tetrahydrofurfurylamine $\xrightarrow{200^\circ C.\pm}$ p-Tetrahydrofurfurylaminophenol

Leucoquinizarin + Methylamine $\xrightarrow{75^\circ C.\pm}$ Leuco-1,4-dimethylaminoanthraquinone

(2) Hydroxy aromatic $+ \; R\text{–}NH_2 \xrightarrow[\substack{\text{Alkali bisulfite,} \\ \text{Sulfite of } RNH_2\text{, etc., as catalysts}}]{160^\circ C.\pm} \text{Aryl–}\overset{H}{\underset{|}{N}}\text{–R}$

β-Naphthol + Ethylamine $\xrightarrow[160^\circ C.\pm]{(NaHSO_3)}$ Ethyl-α-naphthylamine

(3) Hydroxy aromatic $+ \; HN\begin{smallmatrix} R^1 \\ R^2 \end{smallmatrix} \xrightarrow{200^\circ C.\pm} \text{Aryl–}N\begin{smallmatrix} R^1 \\ R^2 \end{smallmatrix}$

Resorcinol + Diethanolamine $\xrightarrow{200^\circ C.\pm}$ m-Hydroxy-di-β-hydroxyethylaniline

(4) Hydroxy aromatic + $HN\langle^{R^1}_{R^2}$ $\xrightarrow[\text{A catalyst such as } CaCl_2,\ HCl,\ H_3BO_3, \text{ etc.}]{200°C. \pm}$ Aryl–$N\langle^{R^1}_{R^2}$

(5) Resorcinol + Diethylamine $\xrightarrow[200°C. \pm]{\text{Diethylamine Hydrochloride}}$ m-Diethylaminophenol

F. Aromatic–X + $HN\langle^{R^1}_{R^2}$ $\longrightarrow$ Aromatic–$N\langle^{R^1}_{R^2}$ wherein X is a group selected from halogen, sulfonic, and nitro.

(1) Sodium anthraquinone-1-sulfonate + β-Methoxyethylamine $\xrightarrow{165°C. \pm}$ 1-β-Methoxyethylamino-anthraquinone

(2) 1-Chloroanthraquinone + Ethanolamine $\xrightarrow{130°C. \pm}$ 1-β-Hydroxyethylamino-anthraquinone

(3) Chlorobenzene + Methylamine $\xrightarrow[225°C. \pm]{\text{Copper Cat.}}$ Methylaniline

(4) 1,2-Dichloro-4,5-dinitrobenzene + Ethylamine $\longrightarrow$ 1,2-Dichloro-4-nitro-5-ethylaminobenzene

II. Reduction Reactions

These reactions are usually carried out best by using hydrogen and a metallic catalyst.

A. Reduction of Nitrogen-Containing Groups

(1) Alkyl NO_2 + $3H_2$ $\xrightarrow{(cat.)}$ Alkyl NH_2

β-Nitropropane + $3H_2$ $\xrightarrow[25°C. +]{(Ni)}$ Isopropylamine

(2) Alkyl CN + $2H_2$ $\xrightarrow{(cat.)}$ Alkyl–CH_2–NH_2

Benzonitrile + $2H_2$ $\xrightarrow[75°C. \pm]{(Ni)}$ Benzylamine

Sebaconitrile $\xrightarrow[100°C. \pm]{(Ni)\ (NH_3)}$ Decamethylene Diamine

(3) Aldoximes + $2H_2$ $\xrightarrow{(cat.)}$ –CH_2–NH_2

Acetaldoxime + $2H_2$ $\xrightarrow[75°C. \pm]{(Ni)}$ Ethylamine

(4) Ketoximes + $2H_2$ $\xrightarrow{(cat.)}$ $-\underset{|}{C}H-NH_2$

Acetone Oxime + $2H_2$ $\xrightarrow[75°C. \pm]{(Ni)}$ Isopropylamine

(5) $-\overset{|}{C}=N-N=\overset{|}{C}- + 3H_2 \xrightarrow{\text{(cat.)}} -\underset{|}{\overset{H}{C}}-NH_2$

Propionaldazine $\xrightarrow[75°C. \pm]{\text{(Ni)}}$ 2 Propylamine

(6) $-\overset{|}{C}=NH + H_2 \xrightarrow{\text{(cat.)}} -\underset{|}{\overset{H}{C}}-NH_2$

Acetaldimine + $H_2 \xrightarrow[75°C. \pm]{\text{(Ni)}}$ Ethylamine

(7) $-\overset{|}{C}=O + NH_3 + H_2 \xrightarrow{\text{(cat.)}} -\overset{H}{C}-NH_2$

Acetone + Ammonia + $H_2 \xrightarrow[75°C. \pm]{\text{(Ni)}}$ Isopropylamine

(8) $-\overset{|}{C}=O + H_2N-R + H_2 \xrightarrow{\text{(cat.)}} -\underset{|}{\overset{|}{C}}-\overset{H}{N}-R$ (R is alkyl or aryl)

Butyraldehyde + Propylamine + $H_2 \xrightarrow[75°C. \pm]{\text{(Ni)}}$ Butyl Propylamine

(9) $-\overset{|}{C}=O + HN\langle^{R^1}_{R^2} + H_2 \xrightarrow{\text{(cat.)}} -\underset{|}{\overset{|}{C}}-N\langle^{R^1}_{R^2}$

Acetaldehyde + Ethylaniline + $H_2 \xrightarrow[25°C. \pm]{\text{(Ni)}}$ Diethylaniline

(10) Acetaldehyde + Ammonia + $H_2 \xrightarrow[75°C. \pm]{\text{(Ni)}}$ Ethylamine

(11) Hydrofurfuramide + $3H_2 \xrightarrow[125°C. \pm]{\text{(Ni)}}$ Furfuryl and Difurfurylamine

Hydrofurfuramide + $nNH_3 + 3H_2 \xrightarrow{\text{(Ni)}}$ Furfuryl and Difurfurylamine (10%)

(12) o-Nitrophenoxy Ketones + $4H_2 \xrightarrow{\text{(cat.)}}$ Phenomorpholines

o-Nitrophenoxyacetone + $4H_2 \xrightarrow[75°C. \pm]{\text{(Ni)}}$ 2-Methylphenomorpholine

(13) Hydrofuramide + $H_2 \xrightarrow[25°C. \pm]{\text{(Adams Cat.)}}$ Trifurfurylamine

B. Reduction of Hetero- and Homocyclic Compounds

(1) Substituted and Unsubstituted Aromatic Amines

p-Phenetidine + $3H_2 \xrightarrow[200°C. +]{\text{(Ni)}}$ 4-Ethoxycyclohexylamine

(2) Substituted and Unsubstituted Pyridine Derivatives

Pyridine + $3H_2 \xrightarrow[150°C. \pm]{\text{(Ni)}}$ Piperidine

(3) Substituted Pyrroles

$$\text{2,5 Dimethylpyrrole} + 2H_2 \xrightarrow[75°C. \pm]{(Ni)} \text{2,5 Dimethylpyrrolidine}$$

$$\text{Skatole} + H_2 \xrightarrow[75°C. \pm]{(Ni)} \text{Dihydroskatole}$$

(4) Substituted and Unsubstituted Quinolines

$$\text{5-Nitroquinoline} + 5H_2 \xrightarrow[\substack{\text{1st step } 25°\text{-}35°C. + \\ \text{2nd step } 75°C. +}]{(Ni)} \text{5-Amino-1,2,3,4-tetrahydroquinoline}$$

C. Catalytic Deamination Reactions

(1) $2RNH_2 \xrightarrow[\Delta]{(cat.)} R\text{-}\overset{H}{N}\text{-}R + NH_3 \text{ and } R\text{-}\overset{R}{N}\text{-}R + 2NH_3$

(2) $\text{Propylamine} \xrightarrow[150°C. \pm]{(Ni)} \text{Dipropylamine} + NH_3$

(3) $\text{Tetrahydrofurfurylamine} \xrightarrow[150°C. +]{(Ni)} \text{Ditetrahydrofurfurylamine} + NH_3$

(4) $\text{Diethylenetriamine} \xrightarrow[225°C. \pm]{(Ni)} \text{Piperazine} + NH_3$

III. Reaction of Ammonia and Primary and Secondary Amines with $\rangle C{=}\overset{|}{C}{-}X$, wherein X is a group such as carboxy, carboxy ester, cyano, carboxy amide, aldehyde, or ketone.

(1) $\text{Acrylonitrile} + 2NH_3 \xrightarrow[0°C.]{} \beta\text{-Aminopropionitrile } (24\%) + HN[-(CH_2)_2CN]_2 \ (70\%)$

(2) $\text{Vinylmethylketone} + \text{Aniline} \xrightarrow[95°C. \pm]{(CH_3COOH)} \gamma\text{-Ketobutylaniline}$

(3) $\text{Methylcrotonate} + \text{Aniline} \xrightarrow[95°C. \pm]{(CH_3COOH)} \beta\text{-Anilino-}\beta\text{-methyl-methylpropionate}$

(4) $\text{Tetrahydroquinoline} + \text{Acrylonitrile} \xrightarrow[95°C. \pm]{(H_2SO_4)} \text{N-}\beta\text{-Cyanoethyltetrahydroquinoline}$

IV. Reaction of Alkylene Oxides, Sulfides, and Imines with Ammonia, and Primary and Secondary Amines

(1) $\text{Ethylene Oxide} + nNH_3 \longrightarrow$ Primary, Secondary, and Tertiary Ethanolamine

(2) $\text{Dibutylamine} + \text{Propylene Oxide} \longrightarrow \beta\text{-Hydroxypropyl-dibutylamine}$

(3) $\text{Ethylaniline} + \text{Ethylene Oxide} \xrightarrow[170°C. \pm]{} \beta\text{-Hydroxyethyl-ethylaniline}$

This process takes place in most of the types of reactions illustrated, particularly if the temperature is 150°C. or higher.

The outline given here covers largely methods having preparative value. Generally, procedures can be followed or carried out under a variety of conditions and, where catalytic, with a great variety of catalysts. By the proper selection of reaction conditions (time, temperature, concentration of reactions, solvents, and pressure), and a judicious selection of catalyst, the preparation of any particular amine can readily be controlled.

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New Eastman Organic Chemicals

4997	Cyclohexylcarbinol BP 182-185° $CH_2(CH_2)_4CHCH_2OH$...MW 114.18	100 g...	$14.00 C
5571	Cyclopropyl Methyl Ketone BP 109-111° $CH_2CH_2CHCOCH_3$...MW 84.11	500 g...	7.00 D
5568	2,4-Dichlorobenzoic Acid MP 159-161° $Cl_2C_6H_3COOH$...MW 191.02	1 kg...	6.70 E
T 5575	Dichloronaphthalene (Techn.) MP 38-53° $C_{10}H_6Cl_2$...MW 197.06	3 kg...	4.05 G
P 5570	5-Diethylaminopentanone-2 (Pract.) BP 200-202° $(C_2H_5)_2NCH_2CH_2CH_2COCH_3$...MW 155.15	500 g...	7.00 D
P 5573	Diindene (Pract.) MP 50-53°	500 g...	4.25 D
P 5579	3,4-Epoxy-1-butene (Pract.) BP 66-67° $OCH_2CHCH{:}CH_2$...MW 70.09	1 kg...	4.35 E
1366	Furoic Acid MP 129-131° $OCH{:}CHCH{:}CCOOH$...MW 112.08	100 g...	3.50 C
P 5574	Hydrindylphenol (Pract.) MP 86-88° $C_9H_9C_6H_4OH$...MW 210.28	500 g...	4.25 D
5584	3-Nitro-1,2-dimethylbenzene MP 10-12.5° $NO_2C_6H_3(CH_3)_2$...MW 151.16	100 g...	3.00 C
4825	n-Octadecane MP 27-28.5° $CH_3(CH_2)_{16}CH_3$...MW 250.40	100 g...	2.50 C
5549	p-Phenylazobenzoyl Chloride MP 92.5-94° $C_6H_5N{:}NC_6H_4COCl$...MW 244.67	1 g...	1.00 O
5580	N-Phenylphthalimide MP 208-210° C_6H_4-1,2-$(CO)_2NC_6H_5$...MW 223.22	100 g...	5.00 C